CLAIMS

What is claimed is:

1. A microcapsule comprising one or more internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and further comprising one or more energy absorbing components in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for magnetic, radiofrequency, microwave, or ultrasound than the specific absorption rate of the polymer membrane.

2. The microcapsule of claim 1, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field.

3. The microcapsule of claim 1, wherein the energy absorbing ~~medium~~ component comprises amorphous carbon, graphite, aluminum powder, acetylene black, TWEEN, sodium amyl alcohol, or paraffin oil, and the energy is radiofrequency or microwave.

4. The microcapsule of claim 1, wherein the energy absorbing ~~medium~~ component comprises a spheroid within the microcapsule, and wherein the spheroid contains amyl alcohol, sorbitan monooleate, SMO-20, graphite/oil, or an oil, and wherein the energy is ultrasound.

5. The microcapsule of claim 1, wherein the microcapsule comprises at least one internal aqueous phase and at least one internal hydrocarbon phase.

6. The microcapsule of claim 1, wherein said outer polymer shell comprises glycerol monosterate, glycerol monooleate, glycerol monolaurate, glycerol dioleate, glycerol distearate, cholesterol, stigmasterol, phytosterol, campesterol, lecithins, polyvinyl pyrrolidone, polyvinyl alcohols, hydrocolloids, polyethylene glycol 400-20000 daltons, dextran 1000-100000 daltons, polyvinylpyrrolidone, polyvinyl alcohols or combinations thereof.

7. The microcapsule of claim 1, wherein one of the internal liquid phases contains a drug or drug precursor.

8. The microcapsule of claim 1, wherein a first internal liquid phase contains a drug precursor, and a second internal liquid phase immiscible with the first internal liquid phase contains an activator of the drug precursor.

9. The microcapsule of claim 7, wherein said drug or drug precursor is an anti-cancer drug or anti-cancer drug precursor.

10. The microcapsule of claim 9, wherein said anti-cancer drug is cis-platin, doxorubicin, daunorubicin, diaziquone, paclitaxel, aziridinylbenzoquinone, muramyl-tripeptide, 5-fluorouracil, cyclophosphamide, melphalan, dacarbazine, methotrexate, cytarabine, azaribine, mercaptopurine, thioguanine, vinblastine, vincristine, bleomycin, prednisone, ethinyl estradiol, diethylstilbestrol, tamoxifen, testosterone propionate, or fluoxymesterone.

11. The microcapsule of claim 7, wherein said drug or drug precursor is an anesthetic.

12. The microcapsule of claim 11, wherein said anesthetic is cocaine, procaine, or lidocaine.

13. The microcapsule of claim 7, wherein said drug or drug precursor is a systemic antibiotic.

14. The microcapsule of claim 13, wherein said antibiotic is a penicillin, vancomycin, a cephalosporin, erythromycin, ampicillin, amoxicillin, chloramphenicol, rifampicin, gentamicin, sulfanilamide, sulfadiazine, sulfamethoxazole, sulfisoxazole, sulfacetamide, para-aminobenzoic acid, streptomycin, or isoniazid.

15. The microcapsule of claim 7, wherein said drug or drug precursor is a systemic antifungal.

16. The microcapsule of claim 15, wherein said antifungal is nystatin, or amphotericin B, or griseofulvin.

17. The microcapsule of claim 7, wherein said drug or drug precursor is a systemic antiviral.

18. The microcapsule of claim 17, wherein said antiviral is idoxuridine, iododeoxuridine, riboviran, or amantidine.

19. The microcapsule of claim 7, wherein said drug or drug precursor is an anti-parasitic.

20. The microcapsule of claim 7, wherein said drug or drug precursor is an anti-inflammatory.

21. The microcapsule of claim 7, wherein the drug or drug precursor is a hormone, a steroid, hydrocortisone, dexamethasone, a systemic quinolone, an aminoglycoside, an antidote, an anti-cholinesterase, a metal poisoning antidote, a cytotoxic agent, an immunomodulator, a cytokine, an interleukin, an alpha-antitrypsin, a bone metabolism regulator, a hypercalcemic agent, a cardiovascular agent, a beta blocker, a cerebral vasodilator, a cerebral metabolic enhancer, a colony stimulating factor, a granulocyte-colony stimulating factor, a granulocyte macrophage-colony stimulating factor, a vasopressor, a local diabetic agent, a CT scan enhancer, an angiocardiography agent, an adenosine deaminase deficiency agent, a gonadotropin inhibitor, an adrenal cortical steroid inhibitor, a gonadotropin releasing hormone stimulant, a urofollitropin, a muscle relaxant, a neuromuscular blocking agent, a prostaglandin analog, a prostaglandin, a prostaglandin inhibitor, a respiratory therapy agent, an anticholinergic, a beta andrenergic stimulator, metoclopramide, tetrahydrocannabinol or a sympathomimetic.

22. The microcapsule of claim 7, wherein said drug or drug precursor is a thrombolytic agent.

23. The microcapsule of claim 22, wherein said thrombolytic agent is urokinase (uPA), tissue plasminogen activator (tPA) or streptokinase.

24. The microcapsule of claim 2, wherein the magnetic particles comprise oxides of iron, nickel and zinc.

25. The microcapsule of claim 2, wherein the magnetic particles comprise about 66 wt % Fe_2O_3, about 9 wt % NiO, and about 25 wt % ZnO.

26. The microcapsule of claim 2, wherein the magnetic particles comprise Fe_3O_4, oxides of copper, gold, silver or combinations thereof.

27. The microcapsule of claim 2, wherein the magnetic particles comprise a ceramic coating.

28. The microcapsule of claim 2, wherein the magnetic particles comprise a methacrylate, alginate, dextran, polyacrylate, or polyvinyl pyrrolidone coating.

29. The microcapsule of claim 2, wherein the magnetic particles have a Curie temperature of from about 41°C to about 95°C.

30. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 1 to about 500 microns.

31. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 300 to about 500 microns.

32. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 50 to about 300 microns.

33. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 30 to about 50 microns.

34. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 20 to about 30 microns.

35. The microcapsule of claim 1, wherein the microcapsule has a diameter of from about 1 to about 20 microns.

36. The microcapsule of claim 1, wherein the microcapsule is further defined as containing a radiocontrast media.

37. The microcapsule of claim 34, wherein the radiocontrast media is a halogenated oil.

38. The microcapsule of claim 37 wherein the radiocontrast media is halogenated poppy seed oil, cotton seed oil, soybean oil, safflower oil, corn oil, sunflower seed oil, sesame seed oil, or canola oil.

39. The microcapsule of claim 37, wherein the radiocontrast media is iodinated poppy seed oil.

40. The microcapsule of claim 1, contained in a pharmaceutically acceptable solution.

41. A composition comprising microcapsules, and wherein said microcapsules comprise two or more internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and further comprising one or more magnetic particles in an internal liquid phase in contact with the outer membrane, wherein the magnetic particles have a Curie point higher than the melting temperature of the polymer membrane; and further wherein a first portion of said microcapsules contain magnetic particles with a first Curie point, and a second portion of said microcapsules contain magnetic particles with a second Curie point, and further wherein the first Curie point is different than said second Curie point.

42. The composition of claim 41, wherein the microcapsules contain a drug.

43. The composition of claim 42, wherein said first portion contains a different drug than said second portion.

44. A method of controlling the release of a drug comprising:

providing a drug delivery solution comprising microcapsules comprising one or more internal, immiscible liquid phases enclosed within a polymer outer membrane having a melting temperature, and further comprising one or more energy absorbing components in an internal liquid phase in contact with the outer membrane, wherein the energy absorbing component has a higher specific absorption rate for magnetic,

radiofrequency, microwave, or ultrasound than the specific absorption rate of the polymer membrane, and a drug contained in at least one of the internal liquid phases;

administering the drug delivery solution to a subject; and

exposing the microcapsule to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.

45. The method of claim 44, wherein the energy absorbing component is a magnetic particle and the energy is a magnetic field.

46. The method of claim 44, wherein the energy absorbing medium comprises amorphous carbon, graphite, aluminum powder, acetylene black, TWEEN, sodium amyl alcohol, or paraffin oil, and the energy is radiofrequency or microwave.

47. The method of claim 44, wherein the energy absorbing medium comprises a spheroid within the microcapsule, and wherein the spheroid contains amyl alcohol, sorbitan monooleate, SMO-20, graphite/oil, or an oil, and wherein the energy is ultrasound.

48. The method of claim 45, wherein the magnetic particles comprise a mixture of oxides of iron, nickel and zinc, and further comprise a ceramic coating.

49. The method of claim 45, wherein the electromagnetic field is an electromagnetic field with a frequency of from about 20 to about 500 KHz.

50. The method of claim 45, wherein the electromagnetic field is an electromagnetic field with a frequency of from about 85 to about 100 KHz.

51. The method of claim 44, wherein the microcapsules contain a drug precursor in a first internal liquid phase and an activator of the drug precursor in a second internal liquid phase immiscible with the first internal liquid phase and the method further comprises exposing the microcapsules to an energy source effective to mix the immiscible internal liquid phases and increase the kinetics of activation of the drug precursor prior to heating the magnetic particles.

52. The method of claim 51, wherein the energy source is UV light of 220-390 nanometers.

53. The method of claim 44, wherein the microcapsules also contain a radiocontrast medium.

54. The method of claim 53, wherein the radiocontrast media is halogenated poppy seed oil, cotton seed oil, soybean oil, safflower oil, corn oil, sunflower oil, sesame seed oil, or canola oil.

55. The method of claim 54, wherein the microcapsules are administered to a subject and detected at a target site by radiography, prior to heating the internal component.

56. The method of claim 44, wherein the microcapsules are administered to a subject intraarterially, intravenously, intraperitoneally, directly into a tissue, or directly into a tumor.

57. The method of claim 56, wherein the subject is a human.

58. The method of claim 44, wherein the drug delivery solution contains two portions of microcapsules wherein a first portion of the microcapsules have a different specific absorption rate for the energy source than a second portion.

59. The method of claim 58, wherein the first portion and the second portion contain different drugs.

60. A method of treating a tumor in a subject comprising:

obtaining a pharmaceutical composition comprising a plurality of microcapsules in a pharmaceutically acceptable solution, each microcapsule comprising:

one or more immiscible internal liquid phases enclosed in a polymer shell having a melting temperature;

a magnetic particle contained in an internal liquid phase in contact with the polymer shell and having a Curie point higher than the melting temperature of the polymer shell and;

an anti-cancer drug contained in an internal liquid phase;

administering the pharmaceutical composition to the subject in a manner effective to place the microcapsules within or adjacent the tumor; and

applying a magnetic field to the microcapsules effective to heat the magnetic particles to a temperature higher than the melting temperature of the polymer shell, thereby melting at least a portion of the polymer shell and releasing the drug.

61. The method of claim 60, wherein the pharmaceutical composition is infused into an artery upstream of the tumor.

62. The method of claim 60, wherein the microcapsules also contain a radiocontrast agent and the microcapsules are visualized prior to application of the magnetic field.

63. The method of claim 62 wherein the radiocontrast agent is a halogenated oil.

64. The method of claim 60, wherein said method is practiced in conjunction with hyperthermia therapy.

65. The method of claim 60, wherein said anti-cancer drug is cis-platin, doxorubicin, daunorubicin, diaziquone, paclitaxel, aziridinylbenzoquinone, muramyltripeptide, 5-fluorouracil, cyclophosphamide, melphalan, dacarbazine, methotrexate, cytarabine, azaribine, mercaptopurine, thioguanine, vinblastine, vincristine, bleomycin, prednisone, ethinyl estradiol, diethylstilbestrol, tamoxifen, testosterone propionate, or fluoxymesterone.

66. The method of claim 60, wherein said anti-cancer drug is a photodynamic therapy agent.

67. The method of claim 66, wherein said agent is photofrin or dibenzoporphyrin.

68. A composition comprising a microcapsule comprising two or more immiscible liquid phases enclosed in a polymer shell having a melting temperature, a drug, and one or more magnetic particles having a Curie point higher than the melting temperature of the polymer shell, wherein the microcapsule is made by the method comprising:

formulating a first phase comprising a first solvent, a first polymer soluble in the first phase and immiscible in a second phase, a co-solvent, oil, and water;

formulating the second phase immiscible with the first phase, the second phase comprising a second solvent, a second polymer soluble in the second phase and immiscible in the first phase, a surface active agent, and a salt;

the surface active agent having a hydrophilic/lipophilic balance value greater than that of the first polymer;

the second polymer having a hydrophilic/lipophilic balance value lower than that of the surface active agent;

creating an interface between the first and second phases in a manner that limits fluid shear to between about 1 to 100 dynes/cm^2, if carried out under conditions of greater than or about equal to 1 gravity, or between about 2 to 30 dynes/cm^2, if carried out under conditions of less than or about equal to 1 x 10^{-2} gravity, and maintains adsorptive surface characteristics at the interface.

69. A composition comprising microcapsules, wherein said microcapsules comprise one or more internal liquid phases enclosed within a polymer outer membrane having a melting temperature, and further comprising one or more magnetic particles in an internal liquid phase in contact with the outer membrane; and further wherein a first portion of said microcapsules has a polymer outer membrane with a different melting point than a second portion of said microcapsules, and further wherein both the first and second melting points are lower than the Curie point of the magnetic particles.

70. The composition of claim 69, wherein said microcapsules contain a drug in a least one of said internal liquid phases.

71. The composition of claim 70, wherein said first portion of microcapsules contains a different drug than said second portion of microcapsules.

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